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PEG-Symposium “Antiinfektiva-Therapie 2017: Erkennen, Bewerten, Handeln”
Therapie invasiver Mykosen

Prof. Oliver A. Cornely, FECMM

CECAD – Cluster of Excellence
Translational Research

Klinik I für Innere Medizin
Hämatologie – Onkologie – Infektiologie

ZKS Köln
Universität Köln





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Potentielle Interessenkonflikte

- Forschungsmittel:** Actelion, Amplyx, Astellas, AstraZeneca, Basilea, Bayer, F2G, Genzyme, Gilead, GSK, Matinas, Merck/MSD, Medicines Company, MedPace, Miltenyi, Pfizer, Sanofi Pasteur, Scynexis, Seres, Viropharma
- Studienplanung:** Achaogen, Amplyx, Anacor, Astellas, Basilea, Cidara, Da Volterra, F2G, Gilead, Matinas, Menarini, Merck/MSD, Nestlé, Paratek, Scynexis, Seres, Summit, Tetrphase, Vical, Vifor
- Referent:** Astellas, Basilea, Gilead, Merck/MSD
- Firmenanteile:** keine





Checkliste

1. Echinocandin beginnen

- Verzögerung steigert Sterblichkeit um 2,4% pro Stunde

2. erneute Blutkultur zentral/peripher

3. ZVK entfernen

4. Ophthalmoskopie

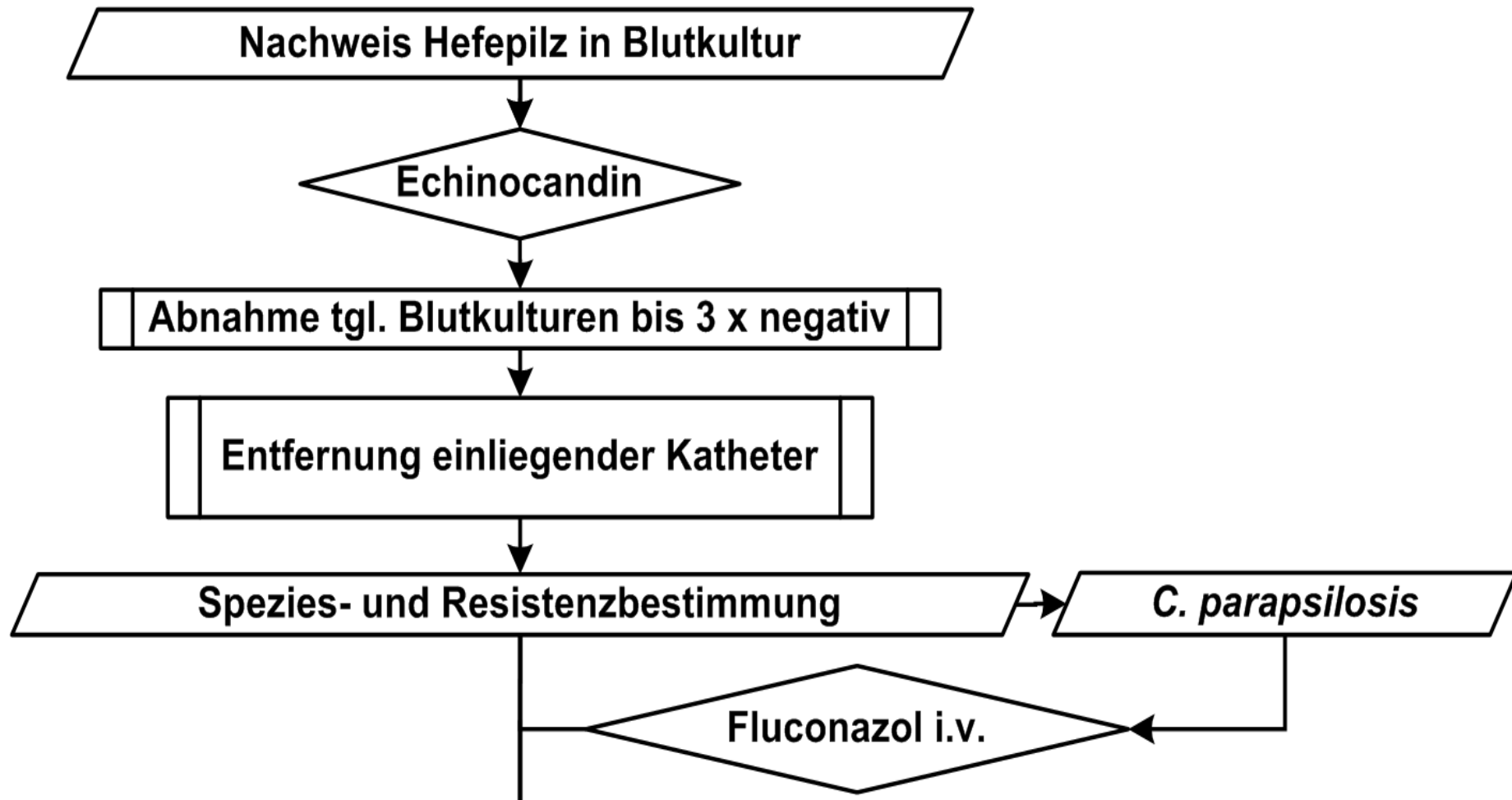
Targeted Treatment of Candidaemia

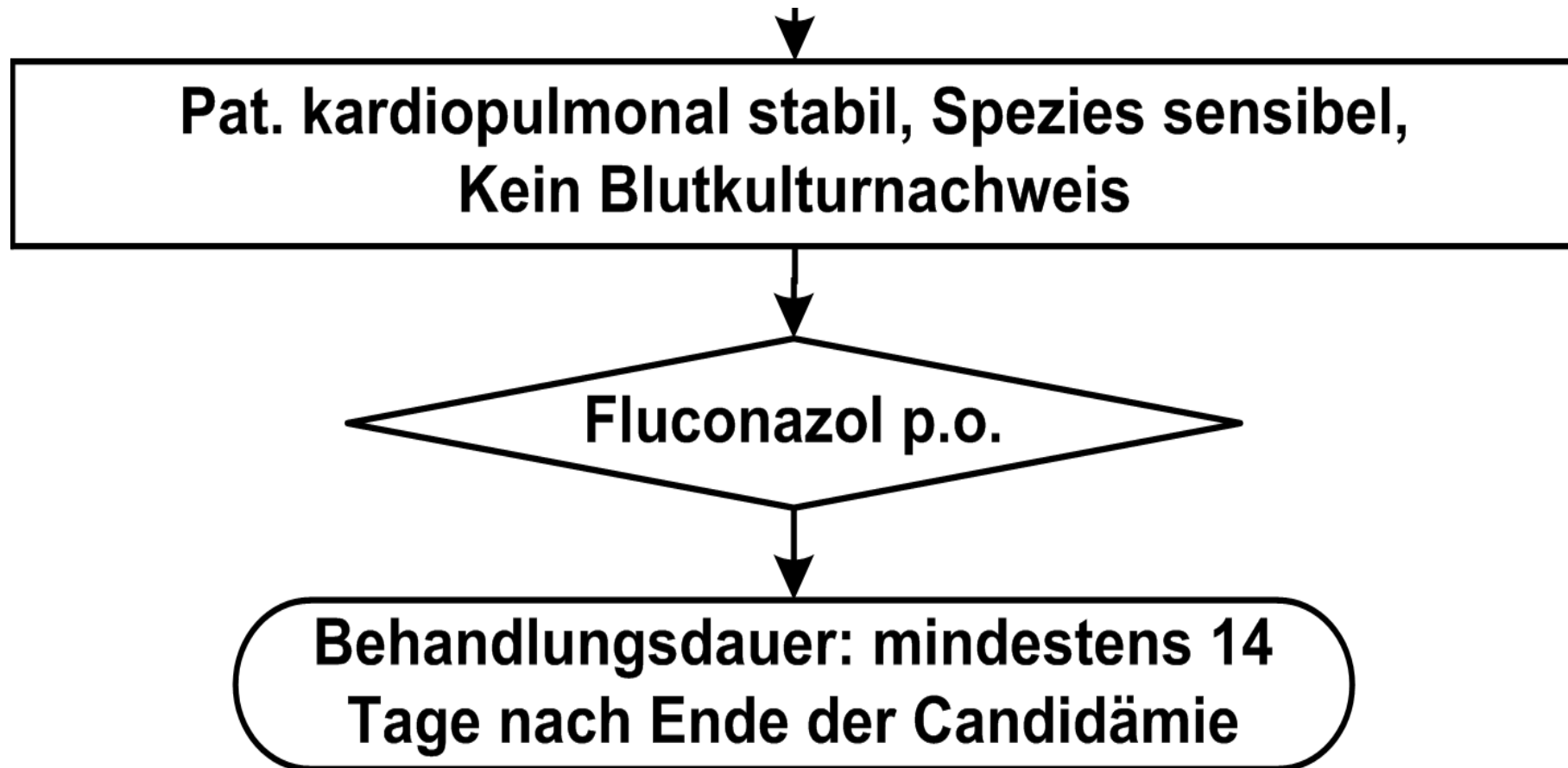
Echinocandins

Compound	SoR	QoE	Reference	Comment
Anidulafungin 200/100	A	I	Reboli NEJM 2007	• Broad spectrum • Resistance rare • Fungicidal • Local epidemiology • C. parapsilosis, C. krusei • Safety profile • Less drug-drug interactions than caspofungin
Anidulafungin war Fluconazol überlegen. Erfolgsrate bei C. albicans mit Anidulafungin höher. Ausnahme: C. parapsilosis				
Caspofungin 70/50	A	I	Mora-Duarte NEJM 2002 Pappas CID 2007	• Largely as above
Micafungin 100	A	I	Kuse Lancet 2007 Pappas CID 2007	• Largely as above • Consider EMA warning label

Recommendations on Catheter Management in Candidaemia

Population	Intervention	SoR	QoE	Reference
Central venous catheter can be removed	Remove indwelling lines (not over a guide wire)	A	IIr	Andes CID 2012
Central venous catheter cannot be removed	Echinocandin, liposomal amphotericin B, or amphotericin B lipid complex	B	IIr	Andes CID 2012 Kucharikova AAC 2010 Kuhn AAC 2002 Mukherjee IJAA 2009 Nucci CID 2010 Rex CID 1995
	Azole, or amphotericin B deoxycholate	D	IIr	Almirante JCM 2005 Andes CID 2012 Leroy CCM 2009 Liu J Infect 2009 Rodriguez CMI 2007 Weinberger JHI 2005



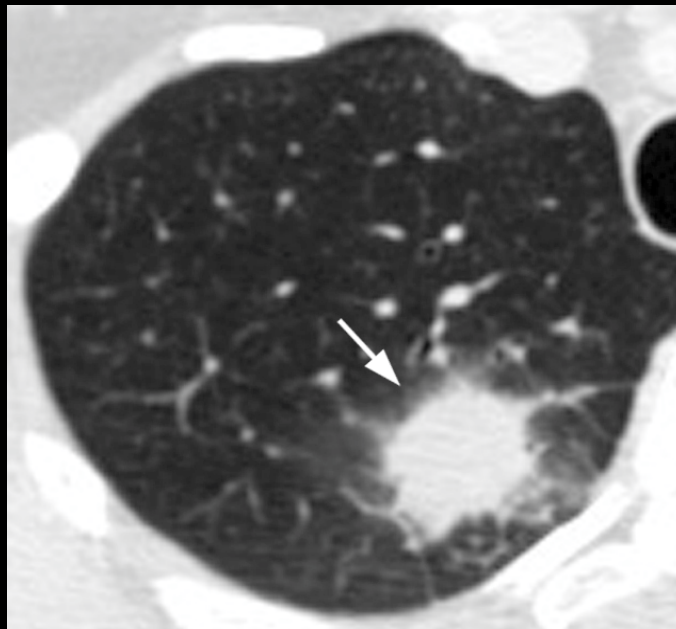




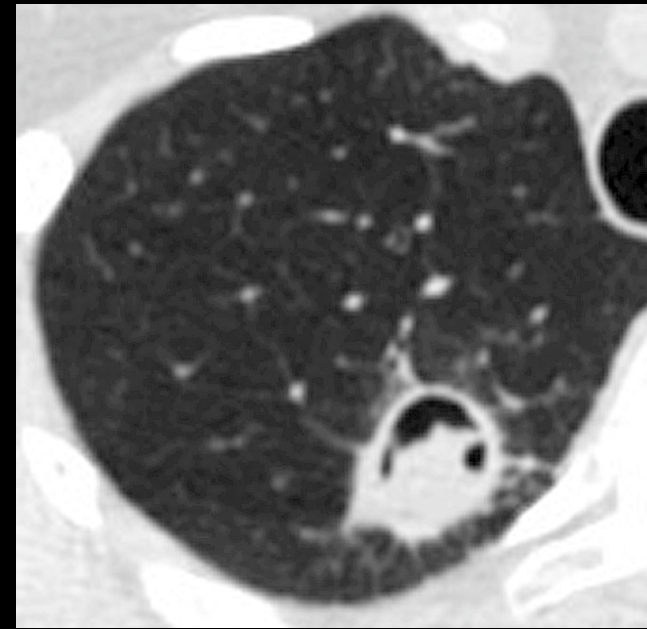
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Aspergillose

Typische CT-Morphologie



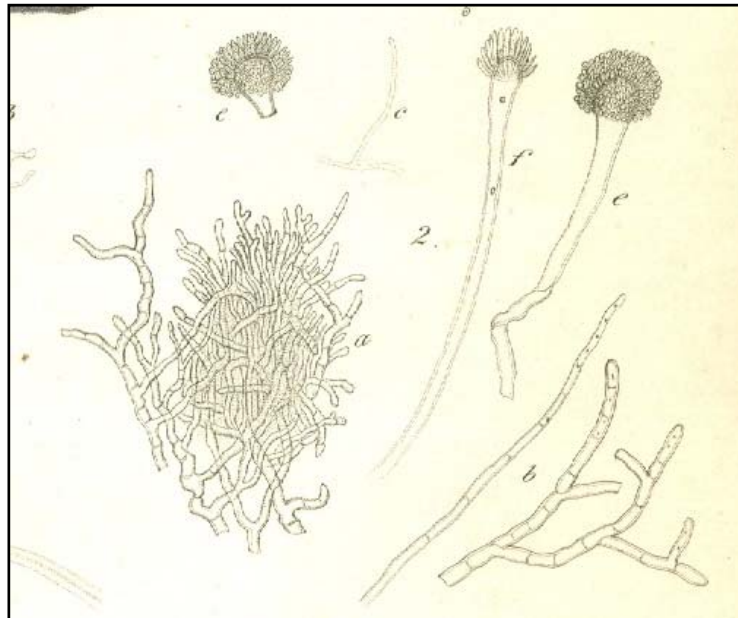
Noduläres Infiltrat mit
umgebendem Halo



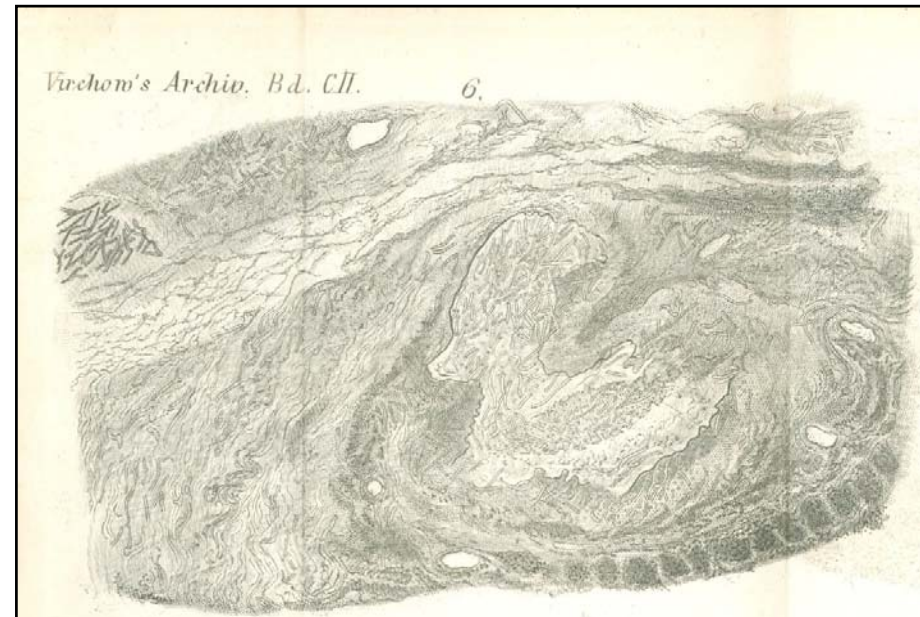
Luftsichel-Zeichen

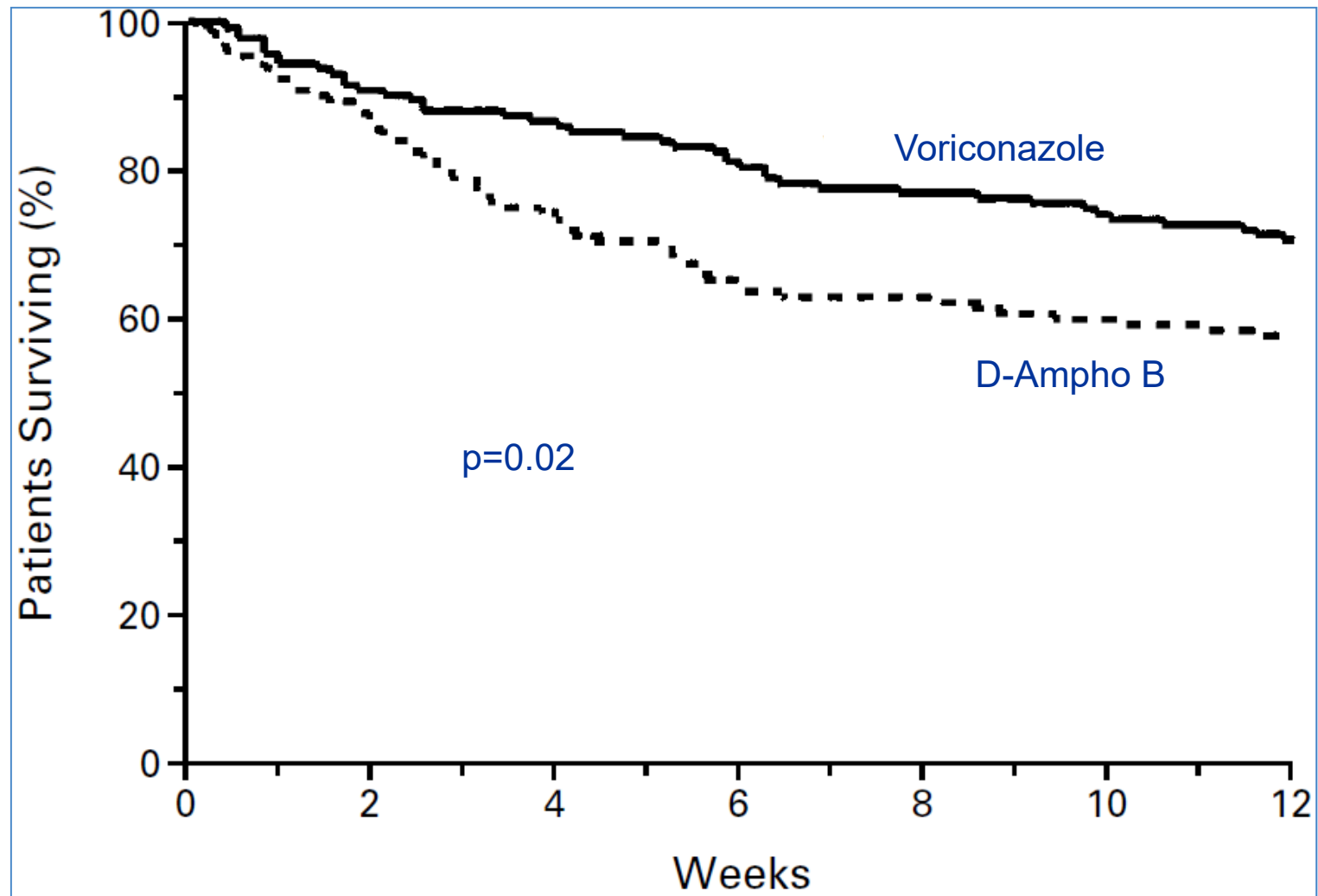


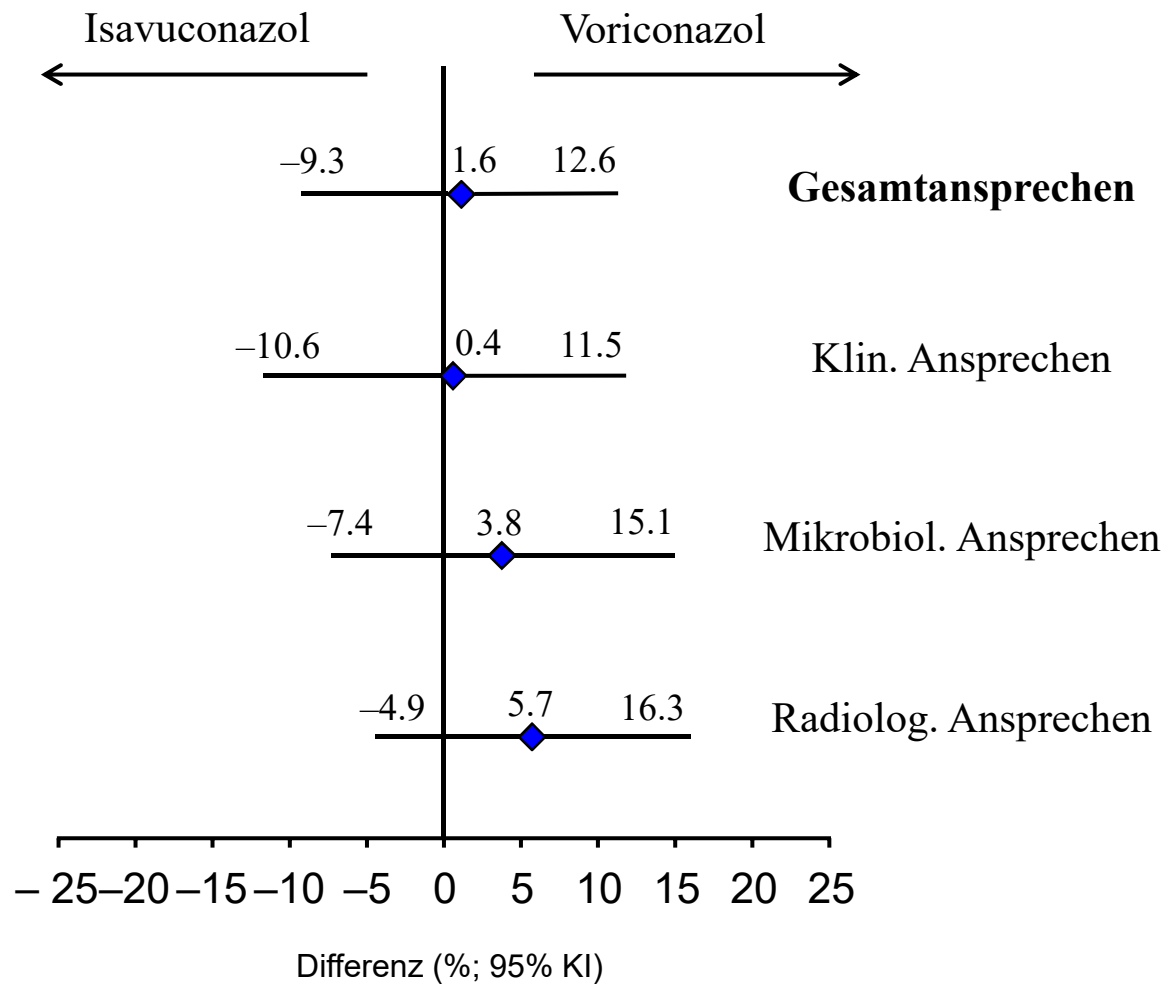
Kultur aus Gewebe



Histologie







ISA	VRC
50/143 (35%)	47/129 (36%)
85/137 (62%)	73/121 (60%)
54/143 (38%)	53/129 (41%)
41/141 (29%)	42/127 (33%)

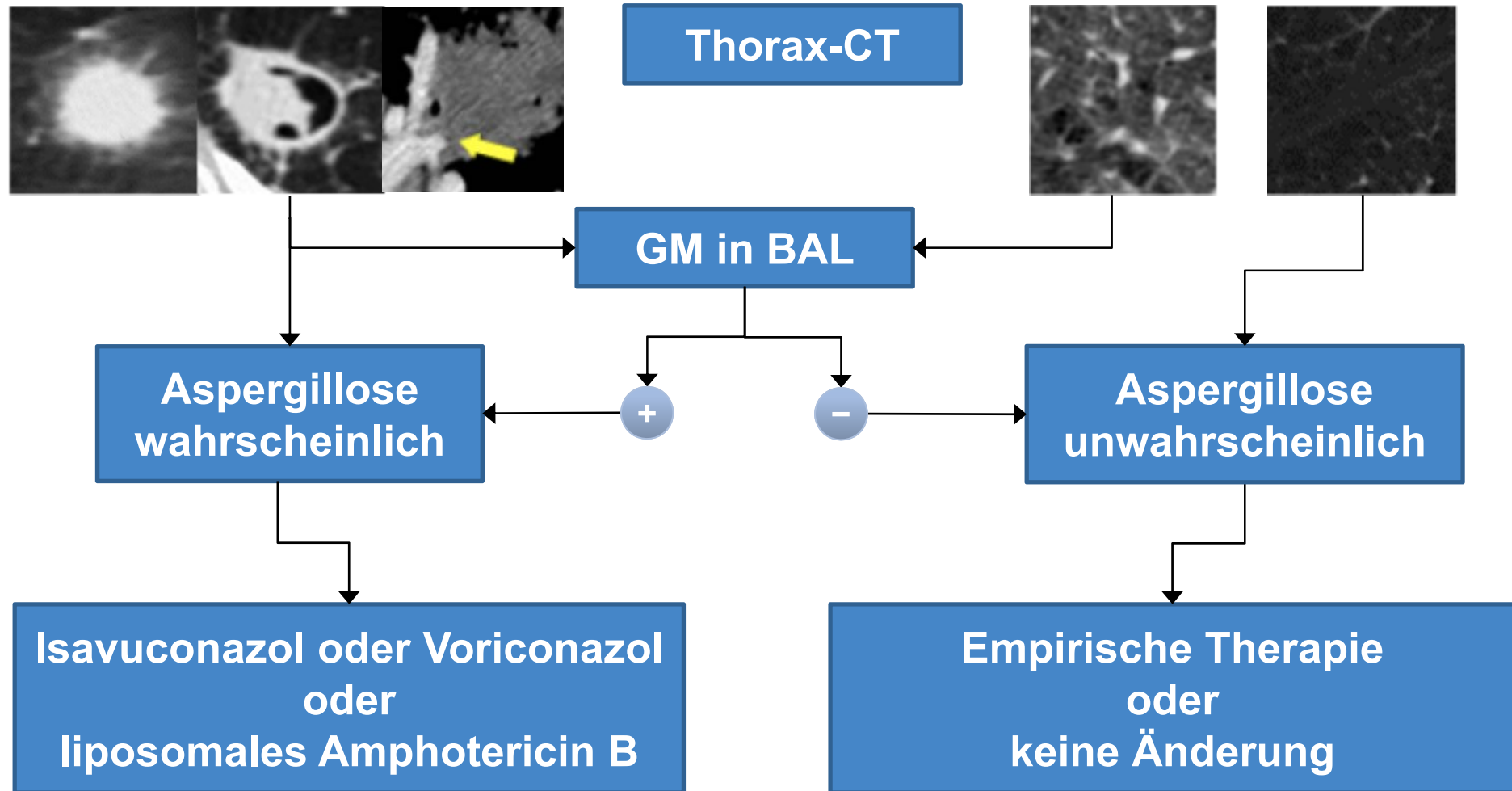


Die häufigsten UEW während der Therapie / Organklassen

System Organ Class	Isavuconazole N = 257	Voriconazole N = 259	p-value
Overall, n (%)	247 (96.1)	255 (98.5)	
Gastrointestinal disorders	174 (67.7%)	180 (69.5%)	
Infections and infestations	152 (59.1%)	158 (61.0%)	
General disorders & admin. site conditions	148 (57.6%)	144 (55.6%)	
Respiratory, thoracic & mediastinal disorders	143 (55.6%)	147 (56.8%)	
Metabolism and nutrition disorders	108 (42.0%)	121 (46.7%)	
Nervous system disorders	95 (37.0%)	89 (34.4%)	
Skin and subcutaneous tissue disorders	86 (33.5%)	110 (42.5%)	0.037
Investigations (abnormal laboratory tests)	85 (33.1%)	96 (37.1%)	
Blood and lymphatic system disorders	77 (30.0%)	82 (31.7%)	
Psychiatric disorders	70 (27.2%)	86 (33.2%)	
Eye disorders	39 (15.2%)	69 (26.6%)	0.002
Hepatobiliary disorders	23 (8.9%)	42 (16.2%)	0.016

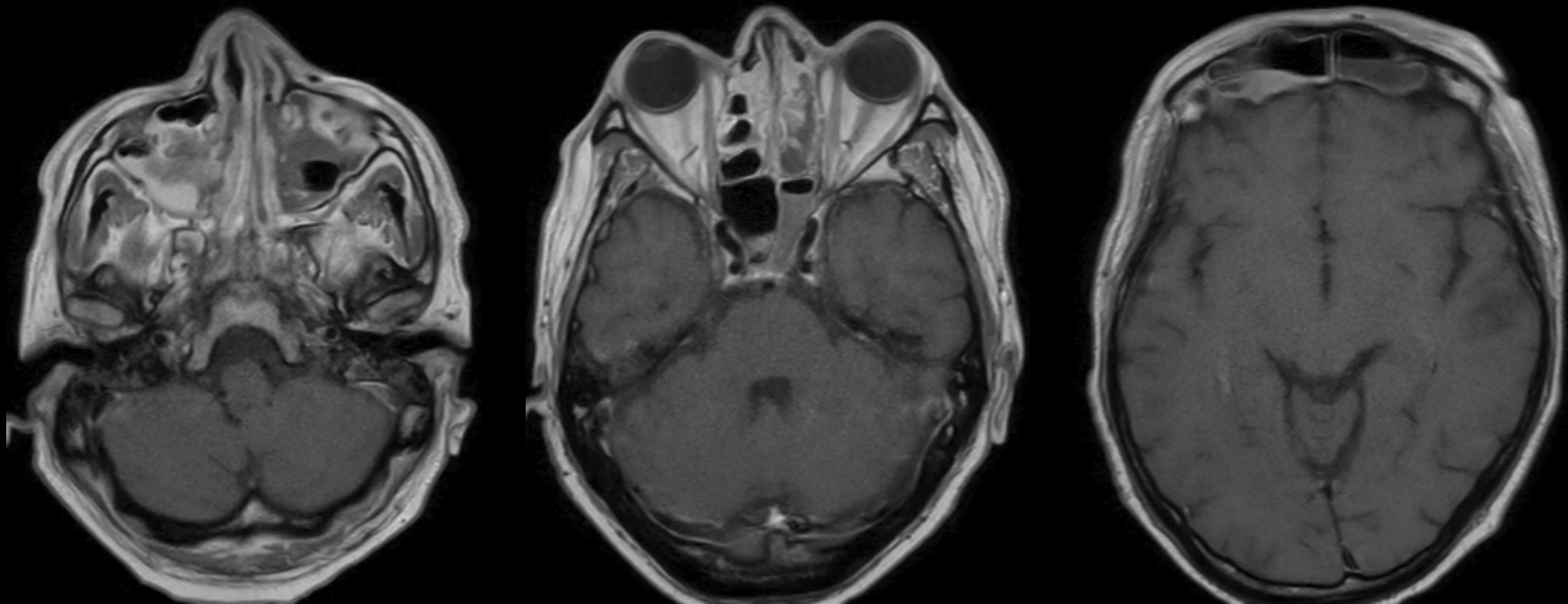


Invasive Aspergillose Diagnose- und Therapie-Algorithmus





- rhinocerebral
 - schlecht eingestellte Diabetiker mit plötzlicher Erblindung
- pulmonal
 - hämatologische Erkrankung mit langer Neutropenie
- Haut-Weichteil
 - traumatische Inokulation bei Unfall, Explosion, Naturkatastrophe



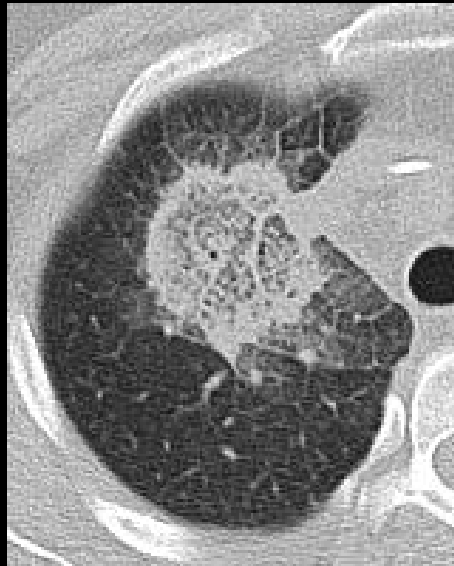


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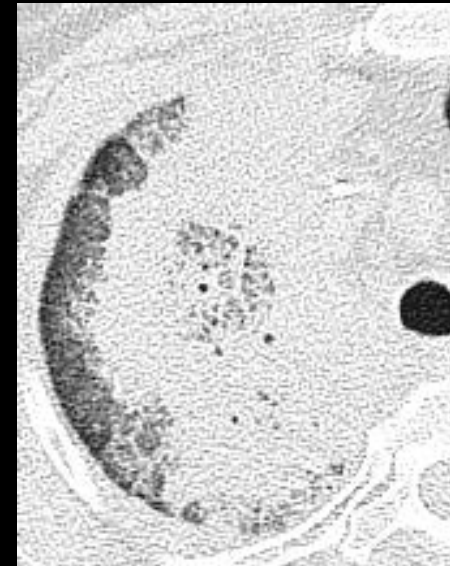
Mukormykose – Inverses Halozeichen



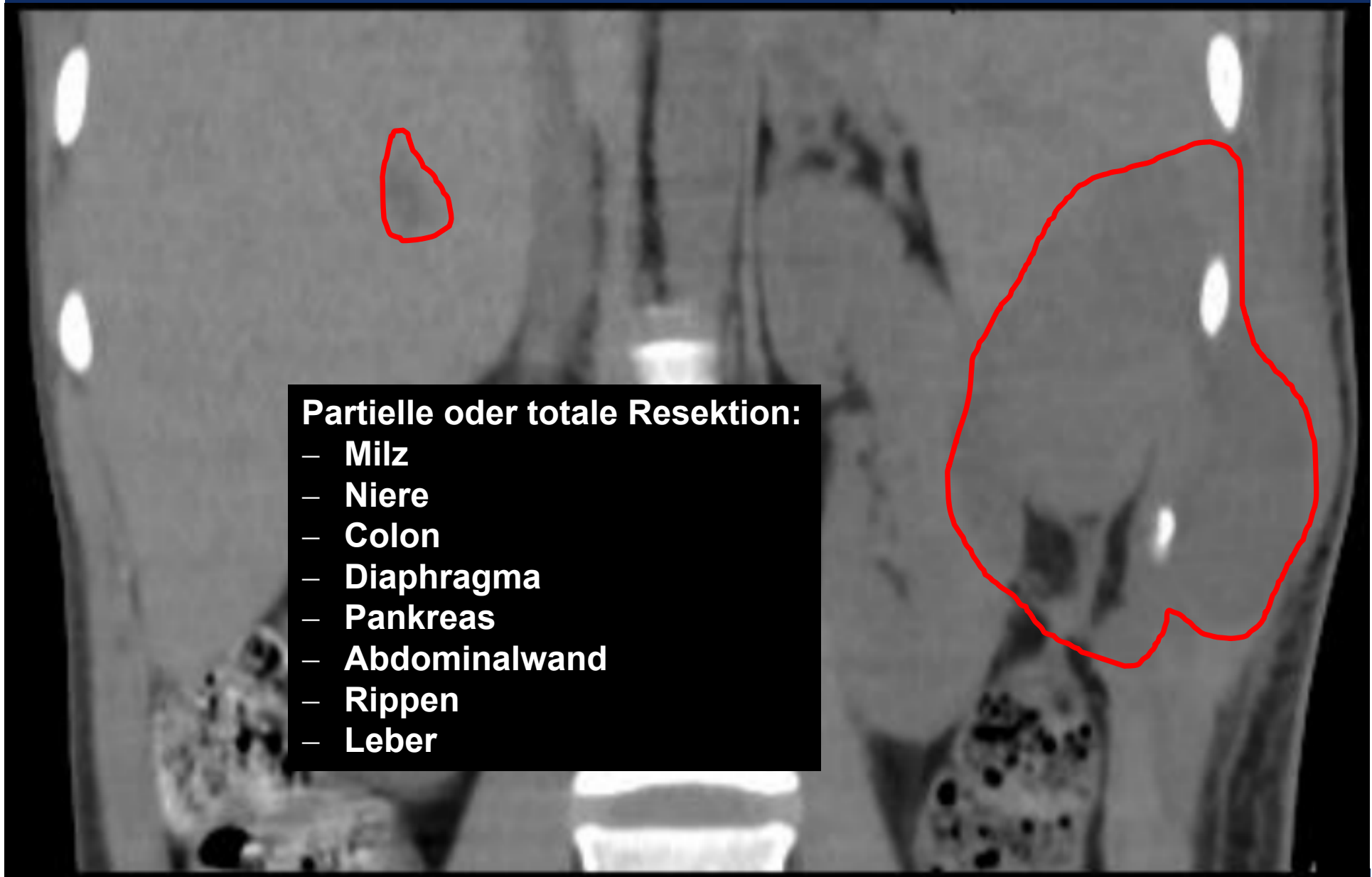
d1



d8



d15



Partielle oder totale Resektion:

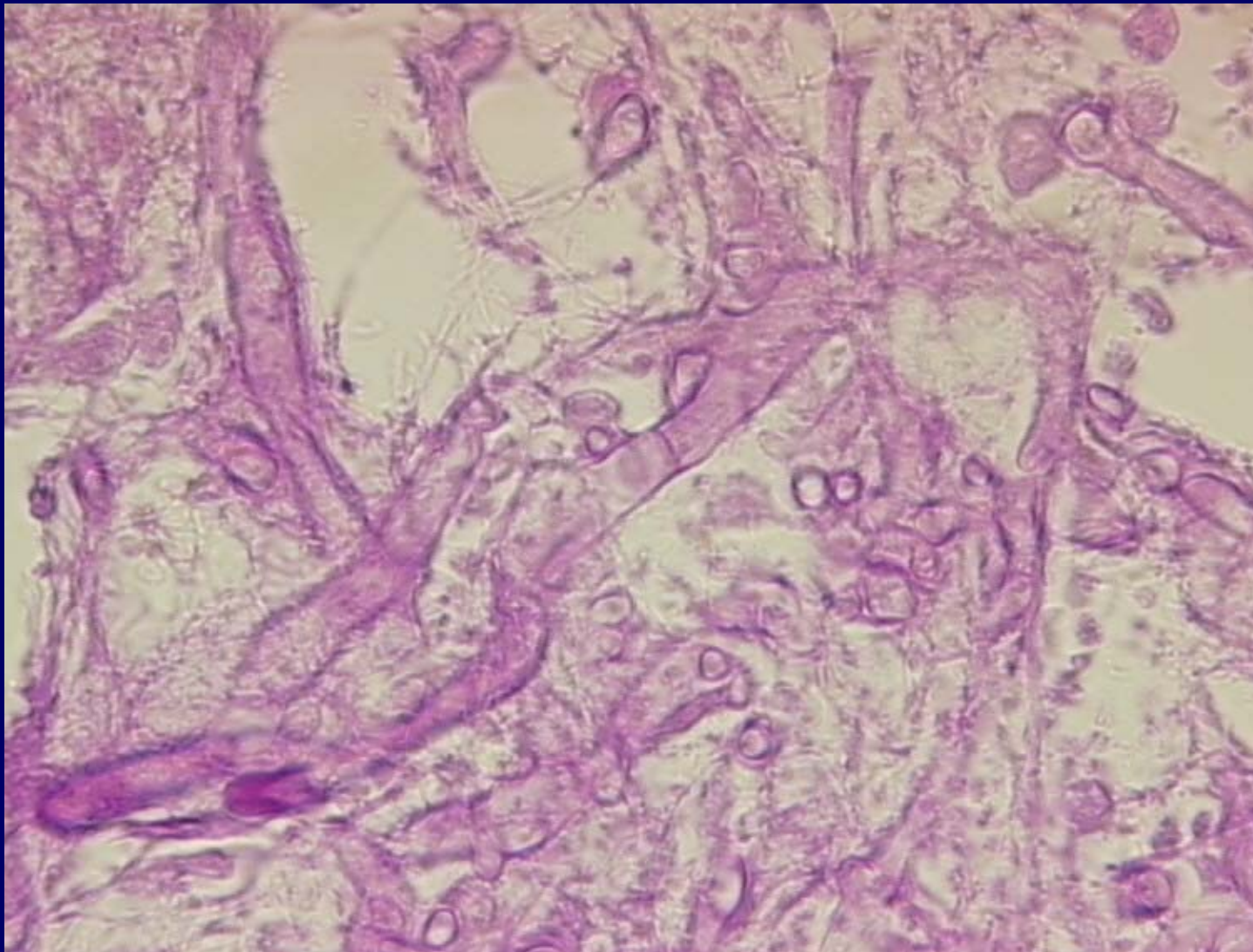
- Milz
- Niere
- Colon
- Diaphragma
- Pankreas
- Abdominalwand
- Rippen
- Leber



1885



Paltauf A. Archiv für pathologische Anatomie 1885; 102 (25): 543-564.





Pop	Intention	Intervention	SoR	QoE	Reference	Comment
Any	To increase survival rates	Surgical debridement	A	II _u	Tedder. Ann Thor Surg 1994 Roden. CID 2005 Chakrabarti. Post Med J 2009 Skiada. CMI 2011 Lanternier. CID 2012 Zaoutis. PIDJ 2007	N=90 N=45 N=59 N=92 paed
Any	To cure and to increase survival rates	Surgery in addition to antifungal treatment	A	II _u	Roden. CID 2005 Greenberg. AAC 2006 Skiada. CMI 2010 Zaoutis. PIDJ 2007	N=470 N=19 N=99 N=92 paed
Any	To cure and to increase survival rates	Amphotericin B, liposomal ≥5 mg/kg	A	II _u	Pagano. Haematologica 2004 Cornely. CID 2007 Rüping. JAC 2010 Shoham. Med Mycol 2010 Skiada. CMI 2011 Lanternier. ICAAC 2012 Ibrahim. AAC 2003 Lewis. AAC 2010	N=4 N=5 N=21 N=28 N=130 N=40 Animal Animal
CNS	To cure	Amphotericin B, liposomal 10 mg/kg, initial 28 Tags	A	III	Ibrahim. AAC 2008 Groll. JID 2000	Animal Animal

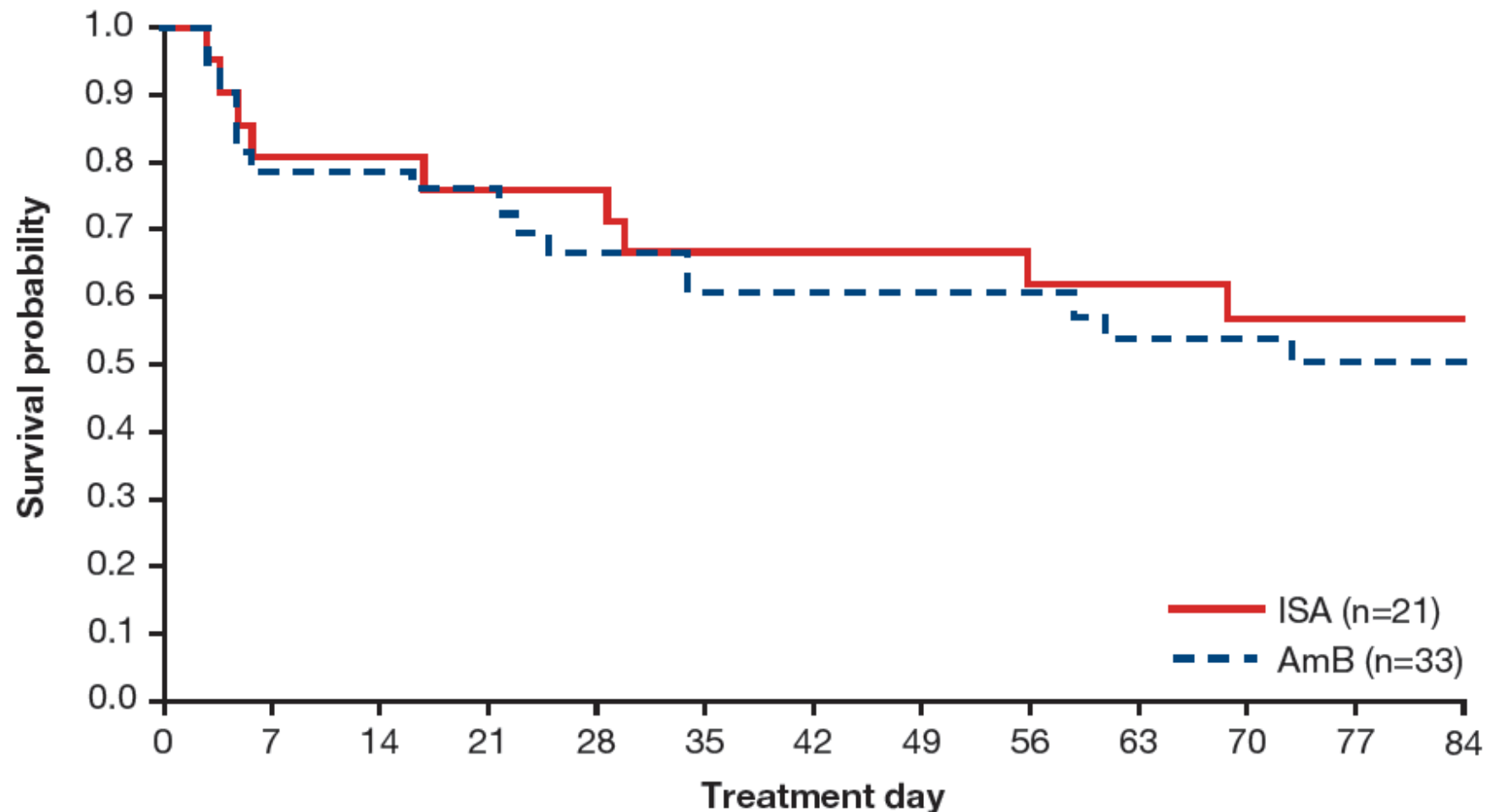
SoR – strength of recommendation, QoE – quality of evidence

ESCMID/ECMM 2013 Clinical Practice Guideline. Cornely OA et al. Clin Microbiol Infect 2014.



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Isavuconazol bei Mukormykose FungiScope™ Matched Control



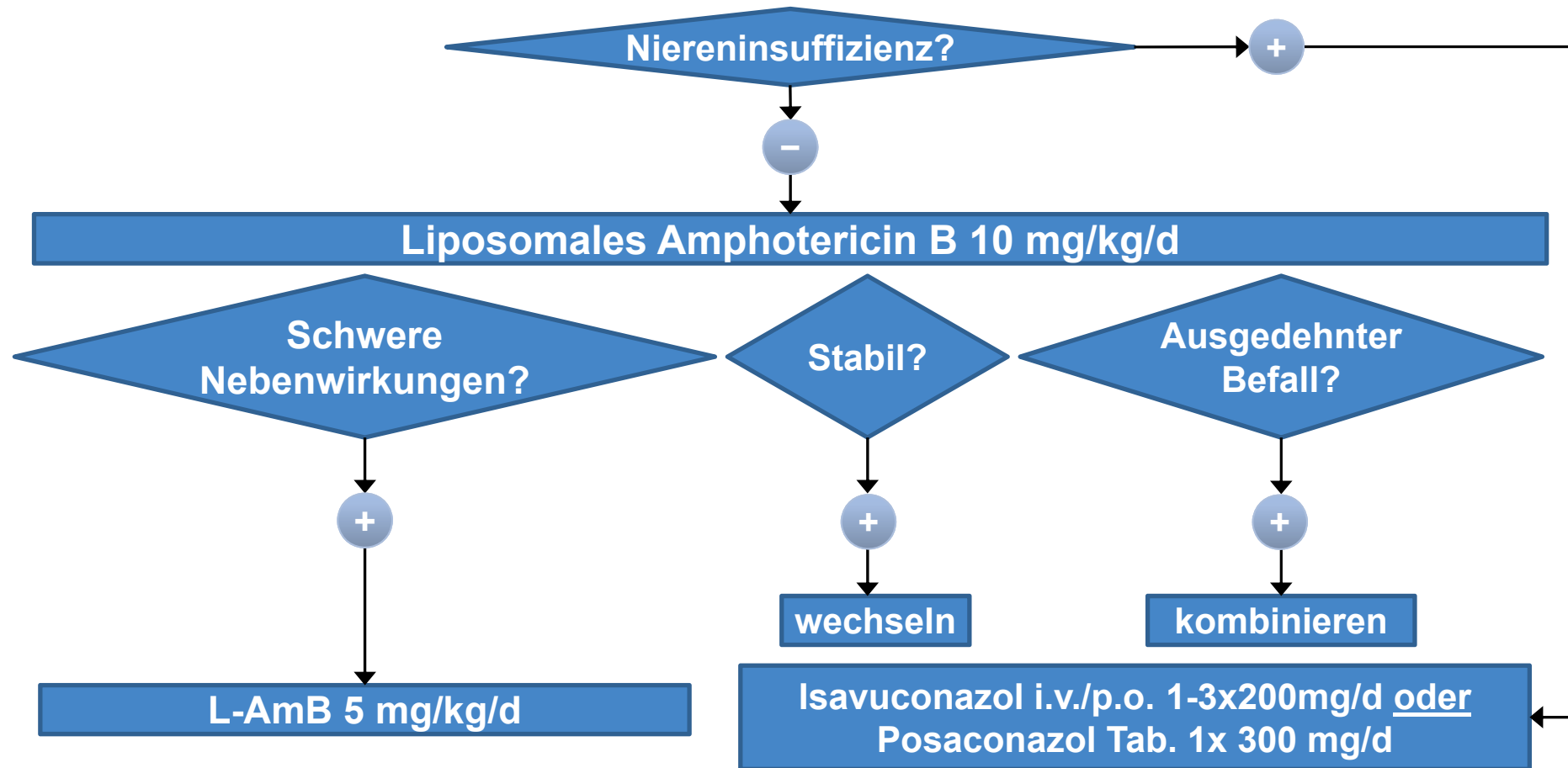
No. of Subjects at Risk

ISA	21	17	17	16	16	14	14	14	14	13	12	12	12
AmB	33	26	26	25	22	20	20	20	18	16	16	14	14

Marty F, ..., Vehreschild MJGT. VITAL-FungiScope. Lancet Infect Dis 2016; 16: 828–37.



Chirurgisches Debridement





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FungiScope register@fungiscope.net



Global Emerging Fungal Infection Registry

Initiated in 2003

ISHAM and ECMM Working Group

www.fungiscope.net



Chair

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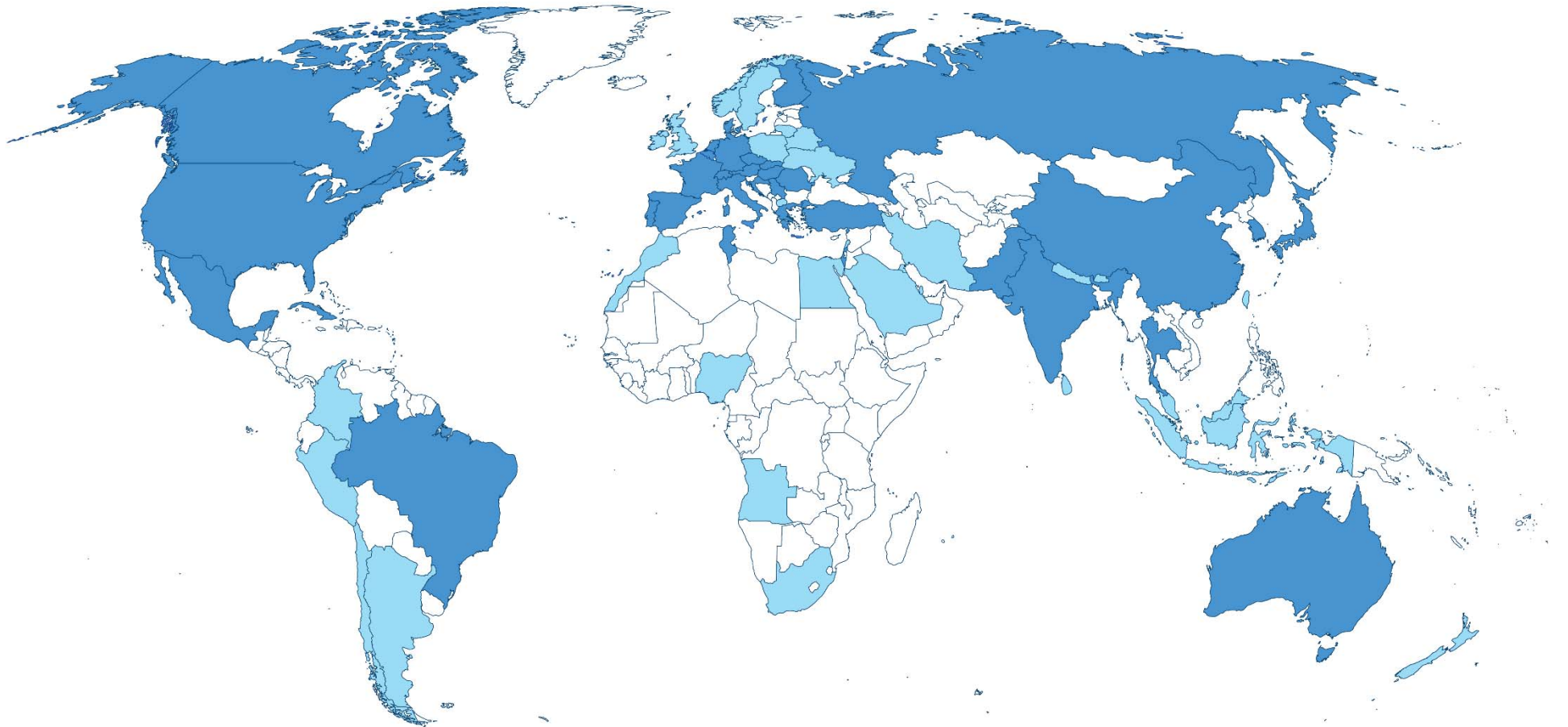
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FungiScope in 66 Ländern





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Clinical Search Engine



www.fungiquest.net

Enter the pathogen you want to search for here:

Search

Culture	PCR	Species	Risk Factors	Site	Empiric Therapy	Targeted Therapy	Surgery IFD	Final Response	Patient alive	Last Observed
✓		Rhizopus microsporus	Chronic renal disease, Diabetes mellitus, ICU, SOT	Lungs	Voriconazole	Liposomal amphotericin B		Stable Disease	Yes	2014
Culture available		Mucor circinelloides	Chemotherapy, Diabetes mellitus, ICU	Lungs	Fluconazole			Deterioration or failure	No	2009
Culture available		Rhizopus arrhizus	Diabetes mellitus, ICU	Lungs				Unknown	Yes	2009
Culture available		Fusarium oxysporum	Chronic pulmonary disease, Diabetes mellitus, ICU	Lungs		Voriconazole		Partial Response	Yes	2009

